



#### General

#### Guideline Title

Consultation and referral guidelines citing the evidence: how the allergist/immunologist can help.

#### Bibliographic Source(s)

Consultation and referral guidelines citing the evidence: how the allergist/immunologist can help. Milwaukee (WI): American Academy of Allergy, Asthma & Immunology (AAAAI); 2011 Feb. Various p.

#### Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: American Academy of Allergy, Asthma & Immunology. Consultation and referral guidelines citing the evidence: how the allergist-immunologist can help. J Allergy Clin Immunol 2006 Feb;117(2 Suppl Consultation):S495-523. [371 references]

## Regulatory Alert

## FDA Warning/Regulatory Alert

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

•	September 26, 2014 – Xolair (omalizumab)	:	: A U.S. Food and Drug Administration (	FDA) review of safety
	studies suggests a slightly increased risk of pr	oblems involving the hear	t and blood vessels supplying the brain ar	mong patients being treated
	with the asthma drug Xolair (omalizumab) than in those who were not treated with Xolair. As a result, FDA has added information ab			
	these potential risks to the drug label.			

## Recommendations

## Major Recommendations

This document includes specific referral guidelines for 14 categories of allergic diseases, along with the rationale for the referral, references, and the type of evidence provided (Tables 1 to 14). The tables are presented alphabetically for easy navigation and do not refer to the prevalence of the individual disease.

Table 1. Allergic Bronchopulmonary Aspergillosis (ABPA)

Referral Guideline	Rationale	Evidence Type
Patients with suspected or proven asthma or cystic fibrosis who have pulmonary infiltrates and peripheral blood eosinophilia	Allergen skin testing and in vitro tests, when correlated with history, can establish the diagnosis of ABPA.	Diagnostic
Patients with known ABPA for management	Allergist/immunologists are specifically trained to manage this disease, and outcomes of such management have been reported by allergist/immunologists.	Indirect outcome (ABPA management)

Table 2. Anaphylaxis (see also "Drug Allergy" [Table 7], "Food Allergy" [Table 8], and "Insect Hypersensitivity" [Table 10] for anaphylaxis due to these agents)

Referral Guideline	Rationale	Evidence Type
Individuals with a severe allergic reaction (anaphylaxis) without an obvious or previously defined trigger	After a severe allergic reaction without a known cause, a trigger should be identified if at all possible. An allergist/immunologist is the most appropriate medical professional to perform this evaluation, which may include skin testing, in-vitro tests, and challenges when indicated (including with exercise-see below). Major triggers for anaphylaxis are foods and food constituents, medications and biologicals, latex, and insect stings. Future avoidance of the identified triggers should prevent subsequent anaphylactic episodes.  Management of idiopathic anaphylaxis by an allergist/immunologist is associated with a reduction in hospitalizations and emergency department visits.	Diagnostic  Indirect outcome (trigger avoidance)  Direct outcome (idiopathic anaphylaxis)
Persons with anaphylaxis attributed to food	Food allergy is the most common cause of anaphylaxis outside of the hospital setting.  Allergist/immunologists use diagnostic modalities to confirm the trigger and use their specific training and clinical experience to educate patients regarding avoidance and immediate management to prevent potentially deadly outcomes.	Diagnostic  Indirect outcome (food avoidance, early interventions)
Exercise-induced anaphylaxis and food-dependent exercise-induced anaphylaxis	After an anaphylactic reaction that appears to have a significant relationship to exercise, it is crucial to be certain whether or not exercise is the cause and to determine whether a food might be involved.	Diagnostic  Indirect outcome (avoidance)
Drug-induced anaphylaxis	Allergist/immunologists use diagnostic agents to confirm the drug responsible for the reaction, if these agents are available (see "Drug Allergy" [Table 7]).	Diagnostic

Table 3A. Asthma Diagnosis

Referral Guideline	Rationale	Evidence Type
Patients with respiratory symptoms suggestive of	Allergist/immunologists perform methacholine challenges, which have	Diagnostic

asthma but with normal PFT results (FEV1 >70% predicted) and no significant reversibility (<12% and -200-mL increase in FEV1)	a high sensitivity for current asthma.	Evidence Type
Exercise-induced symptoms that are atypical or do not respond well to pretreatment with albuterol, nedocromil, or cromolyn	Further objective evaluation and confirmation with pulmonary function testing (including exercise challenge) in conjunction with appropriate allergist/immunologist evaluation will define diagnosis or differential diagnosis.	Diagnostic
Subjects wishing to scuba dive with a history of asthma	There is a theoretic risk of increased barotrauma as well as exercise-induced bronchospasm in patients with asthma who scuba dive. Bronchoprovocation with exercise has been recommended to exclude asthma in scuba divers.	Diagnostic  Indirect outcome (scuba diving avoidance)

PFT = pulmonary function test; FEV1 = 1-second forced expiratory volume

Table 3B. Asthma – Environmental Diagnosis and Management

Referral Guideline	Rationale	Evidence Type
Patients with a history of seasonal or persistent asthma for evaluation of inhalant sensitization to confirm the diagnosis	Exposure to indoor and outdoor allergens may worsen asthma.  Allergy cannot be diagnosed on the basis of history alone. Diagnosis is derived from correlation of clinical history and diagnostic tests, with which allergist/immunologists are facile.  Referral to an asthma specialist is recommended if additional testing is indicated.	Diagnostic
Patients who need management and education concerning environmental triggers	Allergists have familiarity with the wide variety of both indoor and outdoor aeroallergen exposures that have been shown to impact on asthma and respiratory function. Allergists are specifically trained to provide education regarding appropriate avoidance measures. Allergen avoidance can improve asthma.	Indirect outcome (avoidance)
Patients with asthma who experience a worsening of symptoms after a new pet has been introduced into the home	Exposure to furred pets in allergic patients can worsen asthma symptoms. Avoidance of pets in allergic patients can improve asthma.	Diagnostic  Indirect outcome (avoidance)

Table 3C. Asthma Treatment – Immunotherapy

Referral Guideline	Rationale	Evidence Type
Consider referral for allergen immunotherapy for asthmatic patients if there is a clear relationship between asthma and exposure to an unavoidable aeroallergen to which specific IgE antibodies have been demonstrated and:	The efficacy of allergen immunotherapy in the treatment of allergic asthma has been demonstrated in many double-blind, placebo-controlled studies to multiple allergens: e.g., pollen, animal allergen, fungi, dust mite.	Indirect outcome (immunotherapy)
<ul> <li>Poor response to pharmacotherapy or avoidance measures</li> <li>Unacceptable side effects of medications</li> <li>Desire to avoid long-term pharmacotherapy</li> </ul>	Referral to an asthma specialist is recommended if immunotherapy is considered.	

Referral occupience allergic rhinitis  • Long duration of symptoms (perennial or	Rationale	Evidence Type
major portion of the year)		
Consider referral for children with allergic rhinitis because immunotherapy may potentially prevent the development of asthma	Allergen immunotherapy has been shown to reduce development of asthma in children with allergic rhinitis compared with a group of children treated with medication alone. Benefits have also been seen in adults. Immunotherapy may also prevent the development of new allergen sensitivities.	Indirect outcome (immunotherapy)

## IgE= immunoglobulin E

Table 3D. Asthma Treatment: Prevention of Morbidity

Referral Guideline	Rationale	Evidence Type
Patients with asthma who require emergency department care for an acute episode	Allergist care reduces subsequent asthma emergency department visits.  Allergist care reduces subsequent hospitalization.	Direct outcome
Patients with uncontrolled asthma	Allergist care reduces asthma symptoms and improves physical functioning and asthma-related quality of life. Asthma specialist care is associated with improved asthma control.	Direct outcome
Patients with persistent asthma, particularly moderate-to-severe persistent asthma	Inhaled corticosteroid use leads to reduction in asthma symptoms, exacerbations, hospitalizations, and asthma death.	Indirect outcome (controllers)
	Allergist care is more likely to lead to use of asthma controller medications (particularly inhaled corticosteroids).	Indirect outcome (anti-IgE)
	Allergists administer anti-IgE, which prevents exacerbations, improves symptoms, and reduces the use of inhaled steroids in patients with moderate-to-severe asthma.	
Patients who need education on asthma and guidance in techniques for	Use of written action plans improves asthma self-management.	Indirect outcome (education,
self-management	Allergist care is more likely to lead to provision of a written management plan and objective monitoring of asthma using peak flow meters.	action plan)
	Asthma self-management education improves outcomes in children and adults.	
	Allergist care is associated with more effective self-management education and knowledge.	
Patients who use excessive amounts of reliever medications	Excessive short acting beta-agonist use indicates uncontrolled asthma. Allergist care reduces overuse of short acting beta-agonists.	Direct outcome
Patients with severe asthma	Allergist care reduces cost of care for asthma.	Direct outcome

## $IgE = immunoglobulin \ E$

Table 3E. Asthma Treatment: Prevention of Mortality

Referral Guideline	Rationale	Evidence Type
Patients with potentially fatal	Improved Pharmacologic Therapy	

asthma (prior severe, life- referral Guideline threatening episode,	Inhaled steroids have been associated with significant reductions in risk for fatal and near-fatal exacerbation of asthma.	Indirect Evidence Type outcome
intubation)		(inhaled and
	Allergy/immunology physicians prescribe inhaled steroids more frequently than primary	oral steroids)
	care physicians, and patients seen and managed by allergy/immunology physicians are	
	more likely to be taking inhaled steroids regularly.	
	Oral steroid use for attacks reduces the risk of fatal asthma. Patients managed by	
	allergy/immunology physicians are more likely to appropriately receive oral steroids.	
	Immunologic Therapy	
	Allergens may trigger severe and fatal asthma episodes.	Indirect outcome
	Allergy/immunology physicians have expertise in performance and interpretation of skin	(avoidance,
	tests for immediate hypersensitivity, education to encourage aeroallergen avoidance, and	immunotherapy)
	provision of inhalant allergen immunotherapy in properly selected patients.	
	Allergen immunotherapy provides significant clinical benefit, including for alternaria, which	
	has been associated with life-threatening asthma.	
	Anti-IgE therapy has been shown to improve outcomes in high-risk patients.	
	Objective Monitoring of "Poor Perceivers"	
	A major factor contributing to risk for fatal asthma outcomes is under-recognition of asthma; some asthmatic patients are "poor perceivers".	Diagnostic
	Allergy/immunology physicians perform objective measurements of lung function more frequently than other physicians.	
	Action Plans	
	Action plans can reduce asthma mortality. Asthma specialists are more likely to provide	Indirect
	action plans to their patients.	outcome (action plans)

 $IgE = immunoglobulin \ E$ 

Table 3F. Asthma Treatment – Adherence

Referral Guideline	Rationale	Evidence Type
Patients with asthma in whom adherence problems might be limiting optimal control	Patients with a visit to an allergist/immunologist in the prior year were significantly more likely to have been dispensed an optimally effective number of inhaled steroid canisters.  Specialty care is associated with more refills of anti-inflammatory medications.  Patient compliance with national asthma guidelines was higher in patients of specialists.  Misunderstanding of asthma controller medications, which was associated with decreased adherence, was more likely in patients not treated by specialists.	Direct outcome

Referral Guideline	Rationale	Evidence Type
Patients with a history suggesting occupational asthma should undergo testing to confirm the diagnosis of asthma and referral to an allergist for evaluation to establish that the asthma is caused by or triggered by agents at the workplace and to initiate appropriate avoidance therapy.	<ol> <li>History and physical examination are insufficient to confirm occupational asthma, and inaccurate conclusions can easily be drawn. Allergists can interpret spirometry when performed as a baseline, with response to bronchodilator, serial assessment of spirometry or peak flows, and changes in methacholine response during work periods versus off work periods.</li> <li>Allergists can outline the algorithm for the clinical investigation of suspected occupational asthma and interpret other studies to confirm bronchial hyper-responsiveness, including challenges with methacholine, histamine, cold air, or exercise, yet realize that such study results might be negative if performed when the patient is off work and free of symptoms.</li> <li>Allergists can review Material Safety Data Sheets (MSDS), and other specific details of the workplace obtained either through specific questioning, direct observation during an onsite work evaluation or assisting in obtaining an industrial hygiene survey in an effort to identify exposure to possible causal agents. Allergists can arrange and interpret workplace challenges and be able to provide assistance in referring to centers that can perform specific agent laboratory challenges if indicated.</li> <li>The importance of identifying the agent responsible for asthma is that continued exposure can lead to worsening asthma and possibly persistent disease, even after exposure is instituted. Early accurate diagnosis and removal from further exposure to specific work sensitizers carries the best medical prognosis for those with occupational lung disease.</li> </ol>	Diagnostic  Indirect outcome (avoidance)
Consider referral of a worker with asthma for evaluation of workplace exposures that could worsen or exacerbate the asthma.	Exposure to workplace irritants is a known cause of and known exacerbator of asthma.	Indirect outcome (avoidance)

Table 4. Conjunctivitis

Referral Guideline	Rationale	Evidence Type
Patients with prolonged or recurrent manifestations of allergic conjunctivitis  Patients with comorbid conditions (e.g., asthma, rhinitis, recurrent sinusitis)	Allergy cannot be diagnosed on the basis of history alone. Diagnosis is derived from a correlation of clinical history and diagnostic tests, with which allergist/immunologists are experienced. Allergists may help to suspect and diagnose corneal involvement in vernal and atopic keratoconjunctivitis.	Diagnostic
Patients with symptoms interfering with quality of life and/or ability to	A thorough allergy evaluation will complement the patient history and aid in the development of specific treatment plans, including immunotherapy and environmental controls. These treatments may benefit allergic conjunctivitis patients in terms of reduced symptoms, medication use and cost. Allergen immunotherapy can be highly effective in controlling the symptoms of allergic conjunctivitis. Efficacy parameters include symptom and medication scores, conjunctival challenge and	Indirect outcome (avoidance) Indirect outcome (immunotherapy)

function Referral Guideline	immunologic cell markers and cytokine profiles. Allergen immunotherapy may provide lasting benefits after immunotherapy is discontinued.	Evidence Type
Patients who have		
found medications		
to be ineffective or		
have had adverse		
reactions to		
previously		
prescribed		
medications.		

## Table 5. Cough

Referral Guideline	Rationale	Evidence Type
Patients with chronic cough of 3 to 8 weeks or more	Asthma, postnasal drainage, and gastroesophageal reflux disease (GERD) are the most common causes of cough. Spirometry and a chest radiograph have been suggested as the minimum investigations required in the evaluation of chronic cough. Allergists have extensive training to evaluate the upper as well as lower airways in a patient with chronic cough.	Diagnostic
Patients with coexisting chronic cough and asthma	Cough occurs in all asthmatics. However, cough alone is a poor marker of asthma, and asthma might be overdiagnosed in children with cough alone. The allergist can provide expert consultation to both ensure the diagnosis of asthma is correct and maximize therapy in the asthmatic subject (see "Asthma" [Tables 3A through 3G]).	Diagnostic  Indirect outcome (avoidance, pharmacologic, and immunologic therapy)
Patients with coexisting chronic cough and rhinitis	Postnasal drip is the single most common cause of chronic cough. Allergy skin testing and history-testing correlation can differentiate allergic from non-allergic rhinitis (see "Rhinitis" [Table 13A]). Treatment of rhinitis can improve the cough. Treatment of rhinitis by allergists improves patient outcomes (see "Rhinitis" [Table 13A]).	Diagnostic  Indirect outcome (avoidance, pharmacologic, and immunologic therapy)
Patients with chronic cough and tobacco use or exposure	Tobacco smoke exposure clearly increases cough prevalence and exacerbates any pulmonary condition. Chronic cough in cigarette smokers is dose-related. Allergists can assist with active steps to minimize or eliminate tobacco smoke exposure.	Indirect outcome (smoking cessation)

## Table 6A. Atopic Dermatitis

Referral Guideline	Rationale	Evidence Type
To confirm the diagnosis of atopic dermatitis in a patient with dermatitis	Allergist/immunologists are specifically trained to diagnose atopic dermatitis. Defining IgE-mediated sensitivity (by skin or in vitro testing) is useful in the differential diagnosis.	Diagnostic
To identify the role of inhalant allergy in patients with atopic	Aeroallergens can trigger atopic dermatitis. In such patients, environmental control may be helpful.	Diagnostic
dermatitis		Indirect

Referral Guideline	Rationale	Evidence Type (environmental control)
To identify the role of food allergy in patients with atopic dermatitis	Approximately 35% of young children with moderate-to-severe atopic dermatitis have food allergy; the association appears less common in adults, but is possible.	Diagnostic  Indirect outcome (food avoidance)
Patients whose atopic dermatitis responds poorly to treatment	Allergist/immunologists are specifically trained and experienced in managing atopic dermatitis in both children and adults.	Indirect outcome (pharmacologic therapy)
For in-depth exploration of immune mechanisms and etiology of atopic dermatitis	Allergist/immunologists can provide a comprehensive and in-depth evaluation of atopic dermatitis based on their training, expertise and understanding of immune mechanisms.	Diagnostic
Many people with eczema also have asthma or hay fever as children or adults	Good control of atopic dermatitis may theoretically reduce the incidence and/or severity of asthma. Allergist/immunologists are the only specialists trained in the management of both of these (atopic) disorders.	Direct

## IgE = immunoglobulin E

#### Table 6B. Contact Dermatitis

Referral Guideline	Rationale	Evidence Type
To confirm the diagnosis of and identify the cause of	Allergist/immunologists are specifically trained to diagnose contact dermatitis. More allergist/immunologists than dermatologists currently perform patch testing. If an etiology is	Diagnostic
contact dermatitis	defined, avoidance therapy can be initiated.	Indirect outcome
		(avoidance)

## Table 7. Drug Allergy

Referral Guideline	Rationale	Evidence Type
Patients with a history of penicillin allergy who have a significant probability of	The vast majority of patients with a history of penicillin allergy can safely use penicillins if an allergy evaluation, often including a penicillin skin test, is	Diagnostic
requiring future antibiotic therapy	performed.	Indirect outcome
	History alone is inadequate to rule out IgE-mediated allergy to penicillin.	(needed penicillin
	Penicillin skin testing in advance of need does not cause significant resensitization.	treatment)
	Patients who are shown not to be allergic to penicillin might be able to use more appropriate and potentially less toxic antibiotics and/or less expensive antibiotics.	
Patients with a history of penicillin allergy in which a penicillin-class antibiotic is the drug of choice	Skin tests may be negative in such patients, who can then safely receive penicillin. Antibiotic desensitization in skin test positive patients renders them transiently tolerant and induces negative skin test, indicating blocking	Indirect outcome (needed

Referral Guideline	Rationale Ration	penicillin Evidence Type treatment)
Patients with histories of multiple drug allergy/intolerance	Allergist/immunologists provide a comprehensive plan to evaluate the historical adverse drug reactions and provide suggestions on future therapies to minimize risks.	Diagnostic  Indirect outcome (treatment with needed medications)
Patients who may be allergic to protein based biotherapeutics and require use of these materials	Allergist/immunologists perform skin testing using appropriate concentrations and techniques to determine current sensitivity.  For example, insulin desensitization allows for continued insulin therapy in patients with prior systemic reactions.	Diagnostic  Indirect outcome (treatment with needed biotherapeutics)
Patients with histories of adverse reactions to NSAIDs who require aspirin or other	Allergist/immunologists accurately diagnose ASA/NSAID sensitivity through challenge testing.	Diagnostic
NSAIDs	Allergist/immunologists perform ASA desensitization in patients with documented ASA sensitivity who require ASA for other medical conditions.	Indirect outcome (needed NSAID treatment)
	Desensitization in patients with ASA exacerbated respiratory disease may improve the control of both upper and lower respiratory tract disease in these patients.	Indirect outcome (improved respiratory symptoms)
Patients who require chemotherapy medication for cancer or other severe conditions and have experienced a prior hypersensitivity reaction to those medications	Desensitization allows for transient tolerance to chemotherapy medications when there is no alternative treatment.	Indirect outcome (needed chemotherapy)
Patients with a history of possible allergic reactions to local anesthetics	Allergist/immunologists are able to perform skin testing and graded challenge to find a safe local anesthetic for future use. Virtually all patients with histories of reactions to local anesthetics can subsequently tolerate the same or an alternate agent.	Indirect outcome (needed local anesthetic treatment)
HIV-infected patients with a history of adverse reactions to TM-S who need this therapy	Graded TM-S challenges can identify patients who are not currently sensitive to the drug and allow patients with reactions during challenge to subsequently tolerate the drug and safely continue therapy.	Diagnostic  Indirect outcome (needed TM-S therapy)
Patients with a history of reactions to induction agents or to non-penicillin antibiotics	Allergist/immunologists provide a comprehensive plan to evaluate the historical adverse drug reactions and provide suggestions on future therapies to minimize risks. When no alternatives exist, allergist/immunologists can supervise rapid desensitization protocols.	Diagnostic  Indirect outcome (treatment with needed medications)

 $ASA = acetylsalicylic \ acid \ (aspirin); \ HIV = human \ immunodeficiency \ virus; \ IgE = immunoglobulin \ E; \ NSAID = nonsteroidal \ anti-inflammatory \ drug; \ TM-S = trimethoprim-sulfamethoxazole$ 

Table 8. Food Allergy

Referral Guideline	Rationale	Evidence Type
Persons who have limited their diet on the basis of perceived adverse reactions to foods or additives	After allergy evaluation, an estimated one third of perceived adverse reactions to foods and a small fraction of adverse reactions to additives are verified.  Evaluation by an allergist/immunologist is likely to result in an individual's ability to liberalize his or her diet (thereby likely improving nutrition and quality of life).	Indirect outcome (avoiding unnecessary diet restriction)
Persons with a diagnosed food allergy	The allergist/immunologist can apply and interpret diagnostic tests (skin prick tests, serum food-specific IgE assay and oral food challenges) and advise patients on dietary avoidance and emergency care measures. These are important aspects of care because 1) many allergies are not permanent and should be monitored for resolution, and 2) avoidance of allergenic foods and action taken in the event of exposure are difficult to undertake, are prone to errors, and can be dangerous, thus mandating proper education.	Diagnostic  Indirect outcome (food avoidance, early pharmacologic treatment of reaction)
Atopic families with, or expecting, a newborn who are interested in identifying risks for, and preventing, allergy	Family history is the strongest predictor of allergy. A sibling born to a family who already has a child with peanut allergy has a risk for developing that allergy that is more than 10 times greater than that of the general population. Specific guidelines are in place to approach potential allergy in a food-allergy prone child (e.g., breast-feeding and avoidance of allergenic foods). Meta-analyses of studies shows breast-feeding and avoidance of cow's milk/soy in the first year may reduce the risk for allergic disease. The allergist/immunologist can evaluate the risks and explain possible approaches.	Diagnostic  Indirect outcome (prevention of sensitization)
Persons who have experienced allergic symptoms (urticaria, angioedema, itch, wheezing, gastrointestinal responses) in association with food exposure	The allergist/immunologist can perform diagnostic tests such as skin tests, serum IgE test and oral food challenges to determine the cause of the reaction.	Diagnostic  Indirect outcome (food avoidance)
Persons who experience an itchy mouth from raw fruits and vegetables	These symptoms are typical of pollen-food allergy syndrome, or oral allergy syndrome, which can sometimes progress to, or overlap with, more severe allergic reactions. The allergist/immunologist evaluates the reactions to determine the cause and to advise which foods to avoid, identify other potential problematic foods, and assess risks for a severe reaction.	Diagnostic  Indirect outcome (food avoidance)
Infants with recalcitrant gastroesophageal reflux or older individuals with recalcitrant reflux symptoms, particularly if they experience dysphagia	Food allergy may be a cause of infantile reflux, and evaluation for food responsiveness is high (about 40%) for children in whom symptoms do not respond well to standard therapies. Older individuals may have reflux symptoms and possibly dysphagia caused by eosinophilic esophagitis, a disorder that is also commonly food-responsive.	Diagnostic  Indirect outcome (food avoidance)
Infants with gastrointestinal symptoms, including vomiting, diarrhea (particularly	There are a group of food-responsive gastrointestinal disorders of infancy (including food protein induced enteropathy, enterocolitis, and proctocolitis) that	Diagnostic

with blood), near growth, and/or malabsorption whose symptoms are otherwise unexplained, not responsive to medical management, and/or possibly food-responsive (even if screening allergy test results are negative)	Ray be diagnosed, treated and monitored with modalities with which allergist/immunologists are expert, including elimination diets and oral food challenges. Most of the disorders affecting infants cannot be identified with simple screening tests.	Indirect Evidence outcome type (food avoidance)
Persons with known eosinophilic inflammation of the gut	Eosinophilic gastroenteritis, esophagitis, and/or gastroenterocolitis may be food responsive. Patients may improve following identification and elimination of causal foods, modalities for which the allergist/immunologist is expert.	Diagnostic  Indirect outcome (food avoidance)

## IgE = immunoglobulin E

Table 9. Hypersensitivity Pneumonitis (HP)

Referral Guideline	Rationale	Evidence Type
Early referral of patients with suspected hypersensitivity pneumonia to avoid continued environmental exposure resulting in permanent lung injury	Early accurate diagnosis and removal from further exposure to specific sensitizers carries the best medical prognosis for those with HP. Allergists are trained and experienced in environmental exposure history, physical examination, and clinical and laboratory diagnosis of HP.	Diagnostic  Indirect outcome (avoidance)
Diagnostic consultation in patients found to have non-specific interstitial pneumonia (NSIP)	Histologic diagnosis of HP varies from the acute stage, subacute stage, and chronic form. Findings of NSIP should initiate the diagnostic consideration of HP since avoidance of the offending antigen and pharmacologic therapy may result in resolution of the disease or stop the progression of disease.	Diagnostic  Indirect outcome (avoidance and corticosteroids)
Patients with known HP for management	Allergist/immunologists are specifically trained to evaluate environmental exposures, evaluate immunologic results, and treat and follow HP, including oral corticosteroid treatment.	Indirect outcome (avoidance and corticosteroids)

Table 10. Insect Hypersensitivity

Referral Guideline	Rationale	Evidence Type
Consider referral of patients with systemic reactions suspected or possibly caused by insect stings for accurate identification of specific allergen and consideration for venom immunotherapy (or whole-body extract in case of fire ant)	<ul> <li>Up to 3% of the population is at risk for anaphylaxis to insect stings, with approximately 40 documented deaths annually.</li> <li>Patient identification of the correct specific insect species causing an allergic reaction is frequently incorrect.</li> <li>Allergy testing and history-test correlation can more accurately identify specific insects responsible for an allergic reaction and may be helpful in diagnosis, treatment and avoidance recommendations.</li> <li>Skin testing is generally preferred over in vitro testing for the initial evaluation of venom-specific IgE antibodies.</li> <li>Venom immunotherapy (or fire ant whole-body extract)</li> </ul>	Diagnostic  Indirect outcome (avoidance, early pharmacologic treatment of reaction, immunotherapy)

Referral Guideline	Rationale and Rationale are actions in stinging insect—sensitive patients.	Evidence Type
	<ul> <li>Venom immunotherapy can prevent death caused by subsequent stings in hypersensitive patients.</li> </ul>	
Consider referral of patients with systemic reactions suspected or possibly due to biting insects for accurate identification of specific allergen	<ul> <li>Biting insects, such as <i>Triatoma</i> species and mosquitoes, have been identified as a cause of systemic reactions.</li> <li>RAST and skin tests to <i>Triatoma</i> salivary gland extracts and whole-body extracts of other biting insects have been used to identify antigen-specific IgE in sera of hypersensitive patients.</li> <li>Patient education by an allergist/immunologist, including the etiology of their allergy, specific avoidance measures, recognition and treatment of anaphylaxis, and management of local side effects, may reduce patient anxiety and potentially reduce morbidity from future bites.</li> </ul>	Diagnostic  Indirect outcome (avoidance, appropriate pharmacologic therapy)
Consider referral of patients on venom (or fire ant whole-body extract) immunotherapy annually for review of interval history, tolerance of immunotherapy, need for repeat testing, and need for continued therapy	<ul> <li>Regular review of interval history immunotherapy dosing, schedule, and adverse events may contribute to reduced complications of treatment.</li> <li>Regular review may identify new comorbidities or medications that increase the risk of poor outcomes from natural stings or insect immunotherapy reactions.</li> <li>Assessment of reactions to interval stings can be used to monitor the effectiveness of immunotherapy and may be cause for consideration of changes in dose and schedule.</li> <li>The interval between maintenance dose injections can be increased to 4-week intervals during the first year of immunotherapy and eventually to every 6-12 weeks in some patients.</li> <li>Many patients may safely discontinue venom immunotherapy after at least 3-5 years of treatment, although some patients may need to continue immunotherapy indefinitely. An allergist/immunologist with experience in treating insect allergic patients is best suited to facilitate individualized patient decisions.</li> </ul>	Indirect outcome (avoidance, early pharmacologic therapy, immunotherapy)

RAST = radioallergosorbent test

Table 11. Occupational Allergic Diseases

Referral Guideline	Rationale	Evidence Type
Workers 1) who anticipate being exposed to an agent or agents to which they are at risk of allergy development or 2) who are	Workers with congenital urogenital tract abnormalities, spina bifida, health care workers and rubber workers have	Diagnostic
presently being exposed to and are at risk for an allergic reaction to an agent, including rhinitis, conjunctivitis, asthma or	a very high prevalence of latex allergy.	Indirect outcome
eczema, should be referred to an allergist/immunologist for assessment to determine whether the worker might be	Workers with an allergy who may not be able to prevent exposure or are prone to accidental exposure should be	(avoidance)
susceptible to rhinitis, asthma, dermatitis, urticaria or anaphylaxis from the exposure. An example is a worker who will be	educated on self-treatment of asthma, rhinitis, urticaria, eczema and anaphylaxis and have appropriate medications	
exposed to latex and has spina bifida, congenital urogenital tract	to use to control symptoms and signs. Specifically, if the	

abnormalities or a worker with a past history suggestive of latex referral Guideline allergy.	patient has a history of anaphylaxis, prescribing and educating the patient on the proper use of an EpiPen or similar device for self-administration of epinephrine may be life-saving. Allergist/immunologists are specifically trained to educate patients regarding self-treatment of such reactions.	Evidence Type
Workers in whom the cause of occupational induced lung disease, including asthma or hypersensitivity pneumonitis, skin disease or upper respiratory disease such as rhinitis or conjunctivitis, is unable to be determined on the basis of history alone and/or objective evidence is necessary to confirm cause and effect between exposure and disease.	educate patients regarding self-treatment of such reactions.  Skin testing and RAST testing often can identify the cause of a hypersensitivity reaction.  Continued exposure to an allergen may result in progressive lung volume loss, which could be irreversible.  In most cases avoidance of the identified agent is the optimal treatment for occupational diseases.  Correlation of the history with the results of IgE testing helps prevent inappropriate avoidance, which may be suggested by RAST testing alone.  In cases in which the etiology cannot be isolated adequately by history, skin testing or RAST testing, inhalation	Diagnostic  Indirect outcome (avoidance)
Workers with occupational induced rhino-conjunctivitis	challenge, which is the gold standard, can be arranged to provide objective evidence of hypersensitivity reaction.  Workers with rhino-conjunctivitis are at an increased risk to develop asthma. Early avoidance might decrease the risk of further respiratory disease.  By history, skin testing and/or RAST testing and correlating the history and objective findings, the causative agent can often be identified, allowing appropriate avoidance and preventing possible loss of occupation or serious lung disease.  Prognosis of occupational induced respiratory disease is dependent on the extent and duration of exposure.	Diagnostic  Indirect outcome (avoidance
Referral to an allergist/immunologist for career counseling should be considered for adolescents with allergic disease who may be considering careers with exposure to animals or other allergens.	Based on history and relevant studies, allergist/immunologists can assess the future relative risks of such patients in the workplace. These individuals can then be aware of any degree of increased risk of sensitization and be able to modify career plans with suitable advice.	Indirect outcome (avoidance
Workers in occupations with animal exposure who develop rash, upper respiratory symptoms, eye symptoms or lung symptoms	Upper respiratory and lower respiratory, skin and eye symptoms might be due to allergic sensitization to the animals. Allergy testing can confirm sensitization and lead to appropriate interventions.	Diagnostic  Indirect outcome (avoidance
Persons with occupational exposure to food proteins and chronic skin symptoms and/or respiratory symptoms attributable to the work environment	Occupational disease might be related to exposure to food proteins, such as wheat ("Bakers" asthma), or food handling (contact urticaria, contact dermatitis) that is diagnosed through modalities available to the allergist/immunologist. Avoidance is the treatment of choice.	Diagnostic  Indirect outcome (avoidance)

Table 12. Primary Immune Deficiency

Referral Guideline	Rationale	Evidence Type
<ul> <li>Any of the following warning signs:</li> <li>Eight or more new infections within 1 year</li> <li>Two or more serious sinus infections within 1 year</li> <li>Two or more months on antibiotics with little or no effect</li> <li>Two or more pneumonias within 1 year</li> <li>Failure of an infant to gain weight or grow normally</li> <li>Recurrent deep skin or organ abscesses</li> <li>Persistent thrush in the mouth or elsewhere on skin after age 1 year</li> <li>Need for intravenous antibiotics to clear infections</li> <li>Two or more deep-seated infections</li> <li>A family history of immune deficiency</li> </ul>	Frequent infection, unusual infections or unusual complications of usual infections are the most frequent presentation of immune deficiency. Advanced diagnostic strategies are necessary to ensure appropriate diagnosis and treatment.  Allergist/immunologists are trained to diagnose and treat primary immunodeficiency. Immunologic therapy improves immunity, reduces infections, improves organ function, prevents complications, improves quality of life, and may be curative in patients with primary immune deficiencies.	Diagnostic  Indirect outcome (immunologic therapy)

Table 13A. Rhinitis

Referral Guideline	Rationale	Evidence Type
Patients with prolonged or severe manifestations of rhinitis with co-morbid conditions e.g., asthma, recurrent sinusitis, with symptoms interfering with quality of life and/or ability to function or who have found medications to be ineffective or have had adverse reactions to medications.	Allergist-immunologist care for rhinitis is associated with improved quality of life, compliance, and satisfaction with care.	Direct outcome
	Allergy cannot be diagnosed on the basis of history alone. Allergist/immunologists are highly trained to interpret the clinical history and allergy diagnostic test results in both upper and lower airway conditions.	Diagnostic
	Treatment for co-morbid rhinitis may improve asthma outcomes.	Indirect outcome (pharmacologic therapy)
	Allergist/immunologists have familiarity with the wide variety of both indoor and outdoor aeroallergen exposures that have been shown to impact on the upper respiratory tree and have the expertise to provide avoidance education.	Indirect outcome (avoidance)
	Allergen immunotherapy may be highly effective in controlling the symptoms of allergic rhinitis. Allergen immunotherapy may provide lasting benefits after immunotherapy is discontinued.	Indirect outcome (immunotherapy)
Patients with nasal polyps	Allergist/immunologists are specifically trained and experienced in the medical management of nasal polyps, including intranasal steroids, oral steroids, and treatment of complicating sinusitis.	Indirect outcome (pharmacologic therapy)
In addition to the above guidelines, consider referral of the child with allergic rhinitis because of the potential preventive role of allergen immunotherapy in progression of allergic disease.	Allergen immunotherapy has been shown to reduce development of new sensitizations and asthma in children with allergic rhinitis compared to children with allergic rhinitis treated with medication alone.	Indirect outcome (immunotherapy)

Referral Guideline	Rationale	Evidence Type
Patients with chronic rhinosinusitis of any type	This set of conditions related to chronic inflammation of the sinus and contiguous nasal mucosa often co- exists with allergic rhinitis. Allergist/immunologist care is associated with improved outcomes. Allergy immunotherapy is demonstrated to improve outcomes in patients with concomitant allergic rhinitis.	Direct outcome Indirect outcome (immunotherapy)
Patients with chronic or recurrent infectious rhinosinusitis	Many patients with this condition have humoral immunodeficiency, cystic fibrosis, fungal sinusitis, and/or granulomatous diseases. Allergist/immunologists are trained in the evaluation and management of these disorders.	Diagnostic  Indirect outcome (avoidance, pharmacologic, and immunologic therapy)
Patients with chronic eosinophilic rhinosinusitis	This is a chronic inflammatory disease with characteristics of allergic inflammation. It often co-exists with aspirin sensitivity, asthma, and sinus-nasal polyposis. Allergist/immunologists are experts in allergic inflammation and can evaluate and treat both environmental allergy and aspirin sensitivity.	Diagnostic  Indirect outcome (avoidance, pharmacologic, and immunologic therapy)
Patients with allergic fungal rhinosinusitis	This is a chronic inflammatory disease with characteristics of IgE and eosinophilic inflammatory response to fungi in sinuses. Evaluation involves allergy skin testing and other laboratory testing. Management involves medical management, allergen immunotherapy and surgery. Allergist/immunologists are experts in the evaluation and management of allergic diseases, including allergy immunotherapy.	Diagnostic  Indirect outcome (pharmacotherapy, immunotherapy)

Table 14. Urticaria and Angioedema (see also "Anaphylaxis" [Table 2]), "Drug Allergy" [Table 7], and "Food Allergy" [Table 8])

Referral Guideline	Rationale	Evidence Type
Patients with acute urticaria or angioedema without an obvious or previously defined trigger	After a severe allergic reaction without a known cause, a trigger should be identified if at all possible. An allergist/immunologist is the most appropriate medical professional to perform this evaluation, which might include a detailed history, physical examination, skin testing, in vitro testing, and challenges when indicated. Future avoidance of the identified triggers should prevent subsequent anaphylactic episodes.	Diagnostic  Indirect outcome (avoidance)
Patients with acute urticaria or angioedema caused by a presumed food or drug with need for diagnostic confirmation or assistance with avoidance procedures	See "Food Allergy" (Table 8) and "Drug Allergy" (Table 7)	Diagnostic  Indirect outcome (avoidance)
Patients with chronic urticaria or angioedema, i.e., those with lesions recurring persistently over a period of six weeks or more	Allergists and dermatologists have more expertise in caring for patients with urticaria than other specialists. Chronic urticaria often has an autoimmune pathogenesis. Consultation with an allergist/immunologist would include:  1. Reviewing possible etiologic factors (medications, supplements, dietary factors, Animal exposures, physical factors)  2. Possible skin testing	Diagnostic  Indirect outcome (avoidance, pharmacotherapy)

Referral Guideline	Rational essible physical challenges  4. Recommending changes in ingestants or contactants  5. Optimal pharmacotherapy  Allergy/immunology specialists are also knowledgeable of the minimal benefit of multiple laboratory tests in urticaria with an otherwise normal examination.	Evidence Type
Patients who might have urticarial vasculitis or urticarial vasculitis or urticaria with systemic disease (vasculidities, connective tissue disease, rarely malignancies):  a. Lesions last more than 24 hours, leave ecchymotic, purpuric or hyperpigmented residua on or under the skin, or are associated with pain or burning b. Patients who have typical urticaria/angioedema but have signs and symptoms suggestive of systemic illness c. Patients whose symptom control requires regular steroid use	Allergist/immunologist training and expertise should allow appropriate differential diagnosis, determination of the need for biopsy, elimination of a specific inciting agent, and optimal pharmacotherapy.	Diagnostic  Indirect outcome (avoidance, pharmacotherapy)
Patients with chronically recurring angioedema without urticaria	Such patients might have hereditary or acquired angioedema, paraproteinemia, or B-cell malignancies. Allergist/immunologist expertise should allow optimal differential diagnosis, determination of the need for hematology/oncology evaluation, and pharmacologic therapy of hereditary or acquired angioedema due to C1 esterase inhibitor deficiency.	Diagnostic  Indirect outcome (pharmacotherapy)
Patients with suspected or proven cutaneous or systemic mastocytosis	Allergist/immunologists are trained to diagnose and treat this disease.	Diagnostic  Indirect outcome (pharmacotherapy)

# Clinical Algorithm(s)

None provided

# Scope

# Disease/Condition(s)

Allergies and allergic reactions, including:

- Allergic bronchopulmonary aspergillosis
- Anaphylaxis
- Asthma

- Conjunctivitis Cough • Drug allergy • Food allergy
- Dermatitis (atopic and contact)

- Hypersensitivity pneumonitis
- Insect hypersensitivity
- Occupational allergic diseases
- Primary immune deficiency
- Rhinitis, sinusitis, and rhinosinusitis
- Urticaria with or without angioedema (e.g., caused by ingestants, contactants, C1 esterase inhibitor deficiency)

# C ' 1 1'

Guideline Category
Counseling
Diagnosis
Evaluation
Management
Treatment
Clinical Specialty
Allergy and Immunology
Family Practice
Internal Medicine
Pediatrics
Intended Users
Advanced Practice Nurses
Allied Health Personnel
Health Care Providers
Health Plans
Nurses
Patients
Physician Assistants
Physicians

## Guideline Objective(s)

- To assist patients and health care professionals in determining when referral to an allergist/immunologist is needed
- To provide information based on evidence to assist in the decision-making process for the benefit of both patients and the healthcare system

## **Target Population**

Adults and children with allergies or asthma

#### **Interventions and Practices Considered**

#### Diagnosis/Evaluation

- 1. Allergen skin testing for specific immunoglobulin E (IgE)
- 2. In vitro tests for specific IgE
- 3. RAST (radioallergosorbent test)
- 4. History-specific IgE correlation
- 5. Allergy challenges (e.g., to methacholine, histamine, cold air, exercise, food ingestion, drug challenges)
- 6. Pulmonary function tests (e.g., spirometry, peak flow)
- 7. Immune competence

#### Nonpharmacologic Management

- 1. Education regarding appropriate avoidance behavior
- 2. Written management plan (e.g., asthma action plan)
- 3. Industrial hygiene survey assistance
- 4. Education regarding self-monitoring
- 5. Education regarding self-treatment

#### Pharmacologic and Immunologic Management

- 1. Inhaled and oral corticosteroids
- 2. Immunomodulator therapy (e.g., anti-IgE)
- 3. Allergen immunotherapy
- 4. Venom immunotherapy
- 5. Desensitization therapy (e.g., to antibiotics, insulin, aspirin and other nonsteroidal anti-inflammatory drugs)

## Major Outcomes Considered

Sensitivity/specificity of diagnostic tests

Accuracy of diagnosis

Direct and indirect outcomes of interventions performed by the allergist/immunologist

## Methodology

#### Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

## Description of Methods Used to Collect/Select the Evidence

A systematic literature review was conducted in October 2009 on PubMed utilizing a series of key words for each individual guideline topic.

#### Number of Source Documents

Not stated

### Methods Used to Assess the Quality and Strength of the Evidence

**Expert Consensus** 

Weighting According to a Rating Scheme (Scheme Given)

## Rating Scheme for the Strength of the Evidence

- Ia. Meta-analysis of randomized controlled trials
- Ib. Randomized controlled trial
- II. Nonrandomized, controlled intervention study
- III. Observational cohort or case-control study
- IV. Review article, expert opinion

### Methods Used to Analyze the Evidence

Review

Review of Published Meta-Analyses

### Description of the Methods Used to Analyze the Evidence

Not stated

#### Methods Used to Formulate the Recommendations

Expert Consensus

## Description of Methods Used to Formulate the Recommendations

The results from the PubMed search were forwarded to the co-chairs of the original task force that assembled the original document. The co-chairs reviewed the literature and made changes to the content, strength of evidence of the recommendations and references as appropriate. Several areas were updated including: asthma treatment; prevention of morbidity, asthma treatment; prevention of mortality, atopic dermatitis, contact dermatitis, drug allergy, food allergy, primary immune deficiency, rhinitis and urticaria/angioedema.

## Rating Scheme for the Strength of the Recommendations

Not applicable

## Cost Analysis

Published cost analyses were reviewed.

#### Method of Guideline Validation

Not stated

## Description of Method of Guideline Validation

Not applicable

## **Evidence Supporting the Recommendations**

### Type of Evidence Supporting the Recommendations

The evidence included in these guidelines is based on:

- Diagnostic evidence: tests performed or interpreted by allergist/immunologists facilitate diagnosis
- Direct outcome evidence: evidence that intervention by an allergist/immunologist improves outcomes
- Indirect outcome evidence: evidence that interventions performed by allergist/immunologists improve outcomes (evidence to support
  established pharmacologic management will generally not be reviewed)

## Benefits/Harms of Implementing the Guideline Recommendations

#### Potential Benefits

- For many patients with asthma and allergic diseases, working with an allergist/immunologist can assist them in managing their disease and
  preventing morbidity and mortality.
- Providing information based on evidence to assist in the decision-making process benefits both patients as well as the healthcare system.

#### **Potential Harms**

Not stated

## Implementation of the Guideline

## Description of Implementation Strategy

An implementation strategy was not provided.

## Implementation Tools

Quick Reference Guides/Physician Guides

Slide Presentation

For information about availability, see the Availability of Companion Documents and Patient Resources fields below.

# Institute of Medicine (IOM) National Healthcare Quality Report Categories

#### IOM Care Need

Getting Better

Living with Illness

Staying Healthy

#### **IOM Domain**

Effectiveness

Patient-centeredness

## Identifying Information and Availability

## Bibliographic Source(s)

Consultation and referral guidelines citing the evidence: how the allergist/immunologist can help. Milwaukee (WI): American Academy of Allergy, Asthma & Immunology (AAAAI); 2011 Feb. Various p.

## Adaptation

Not applicable: The guideline was not adapted from another source.

#### Date Released

2006 Feb (revised 2011 Feb)

### Guideline Developer(s)

American Academy of Allergy, Asthma and Immunology - Medical Specialty Society

## Source(s) of Funding

American Academy of Allergy, Asthma and Immunology

#### Guideline Committee

Not stated

## Composition of Group That Authored the Guideline

Not stated

#### Financial Disclosures/Conflicts of Interest

Not stated

#### Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: American Academy of Allergy, Asthma & Immunology. Consultation and referral guidelines citing the evidence: how the allergist-immunologist can help. J Allergy Clin Immunol 2006 Feb;117(2 Suppl Consultation):S495-523. [371 references]

Guideline Availability
Electronic copies: Available from the American Academy of Allergy, Asthma, & Immunology Web site
Availability of Companion Documents
The following are available:
<ul> <li>How the allergist/immunologist can help: consultation and referral guidelines citing the evidence. Primary care summary. Electronic copies: Available from the American Academy of Allergy, Asthma, &amp; Immunology Web site</li> <li>When to refer your patient to an allergist/immunologist. Slide set. 28 p. Electronic copies: Available from the American Academy of Allergy, Asthma, &amp; Immunology Web site</li> </ul>
Patient Resources
None available
NGC Status
This NGC summary was completed by ECRI on August 8, 2006. The information was verified by the guideline developer on September 20, 2006. This NGC summary was updated by ECRI Institute on May 22, 2012. This summary was updated by ECRI Institute on November 14, 2014 following the U.S. Food and Drug Administration advisory on Xolair (omalizumab).

### Copyright Statement

A complimentary copy of the guidelines (originally published as a supplement to the Journal of Allergy and Clinical Immunology) can be obtained from the AAAAI Web site at www.aaaai.org

## Disclaimer

#### NGC Disclaimer

The National Guideline Clearinghouseâ, & (NGC) does not develop, produce, approve, or endorse the guidelines represented on this site.

All guidelines summarized by NGC and hosted on our site are produced under the auspices of medical specialty societies, relevant professional associations, public or private organizations, other government agencies, health care organizations or plans, and similar entities.

Guidelines represented on the NGC Web site are submitted by guideline developers, and are screened solely to determine that they meet the NGC Inclusion Criteria which may be found at http://www.guideline.gov/about/inclusion-criteria.aspx.

NGC, AHRQ, and its contractor ECRI Institute make no warranties concerning the content or clinical efficacy or effectiveness of the clinical practice guidelines and related materials represented on this site. Moreover, the views and opinions of developers or authors of guidelines represented on this site do not necessarily state or reflect those of NGC, AHRQ, or its contractor ECRI Institute, and inclusion or hosting of guidelines in NGC may not be used for advertising or commercial endorsement purposes.

Readers with questions regarding guideline content are directed to contact the guideline developer.